REMARKS:

Applicants express gratitude to the Examiner for withdrawal of the rejections under 35 U.S.C. § 102(e). The preceding amendments and following remarks form a full and complete response to the office action dated May 18, 2009. Claims 30-32 have been amended by incorporating the subject matter of claim 3. Accordingly, claim 3 has been cancelled. Claim 33 has been amended by incorporating the subject matter of claims 13 and 14, in the alternative. Accordingly, claims 13 and 14 have been cancelled. No new matter is added.

Response to Rejections under 35 U.S.C. § 112

Claims 2-9, 13-27, 30 and 33 were rejected under 35 U.S.C. § 112, first paragraph as lacking enablement. The Examiner asserts that the specification does not provide enablement for a method of treating hyperproliferative cells *in vivo* comprising the administration of an inhibitor of a receptor tyrosine kinase ligand. The Examiner asserts that the Applicants have not provided objective evidence to show that *in vitro* assays are correlatable to the claimed in vivo effects. Applicants submit that the numerous *in vitro* assays on pages 16-31 of the specification show that the claimed inhibitor inhibits a receptor tyrosine kinase ligand and the sum total of these *in vitro* results is readily correlatable with an *in vivo* effect when administering the claimed inhibitors.

Applicants submit herewith *in vivo* results published in PCT application WO2009/040134 demonstrating successful treatment of hyperproliferative cells in mice by administering a receptor tyrosine kinase ligand inhibitor. The figures show that administering anti-HB-EGF antibodies causes reduced pancreatic tumor (Fig. 37) and

ovarian cancer tumor growth *in vivo* (Fig. 38A-C). Thus, the same tumor fighting effect demonstrated in the *in vitro* results in the Examples correlates with tumor volume reduction *in vivo*. Applicants submit that the objective evidence provided herewith demonstrates the correlation of *in vitro* testing, which is routine and required in drug development, with *in vivo* effectiveness. It is anticipated that this data and conclusions drawn therefrom will be presented in the form a declaration in a supplemental filing.

The present specification provides disclosure on page 9, line 11 to page 11, line 24 that would enable one of skill in the art to determine proper dosages, dosage forms, and routes to administer inhibitors of receptor tyrosine kinase ligands. Thus, based on the above, Applicants submit that the present specification enables one of ordinary skill to use the presently claimed method and respectfully request that the rejections under 35 U.S.C. § 112, first paragraph, be withdrawn.

Response to Rejections under 35 U.S.C. § 102

Claims 2, 15-18, 22, 26-27, and 30-33 were rejected under 35 U.S.C. § 102(b) as being anticipated by Tang et al. (U.S. 5,773,459). Based on the ELISA assay disclosed in col. 19-20, the Examiner asserts that Tang discloses that the drug inhibits the binding of the ligand to the receptor and is therefore inhibiting the ligand. Applicants respectfully disagree.

Tang discloses that "the invention is based upon the discovery and design of compounds that inhibit, prevent, or interfere with the signal transduced by KDR/FLK-1 when activated with by ligands such as VEGF." (col. 8, lines 42-46). There is no mention of inhibiting the EGF ligand in col. 19-20 of Tang. Rather, Tang only discloses

mention of inhibiting the EGF ligand in col. 19-20 of Tang. Rather, Tang only discloses that EGF ligand is prepared and then incubated with the cells for five minutes, after which EGFR kinase activity is measured using ELISA. Thus, in accordance with the above-captioned disclosure, Applicants submit that Tang does not disclose or suggest using a drug that inhibits binding of ligand to the receptor, but instead discloses using a drug that inhibits, prevents, or interferes with the signal transduced by EGFR when it is activated by the ligand. Moreover, the subject matter of claim 3, which the Examiner does not contend are anticipated by Tang, has been incorporated into claims 30-32 and the subject matter of claims 13 and 14, which the Examiner also does not contend are anticipated by Tang, has been incorporated into claim 33. Thus, based on the above, Applicants submit that Tang does not anticipate the present claims and respectfully request that the rejections under 35 U.S.C. § 102(b) be withdrawn.

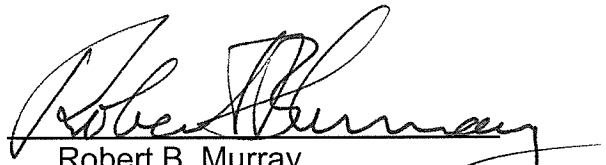
Claims 2, 6, 8-9, 15-19, 22, 26-27, and 30-33 were rejected under 35 U.S.C. §102(e) as being anticipated by Lee (U.S. 6,537,988). The Examiner asserts that Lee discloses the administration of epidermal growth factor inhibitors (see col. 10, lines 30-35) and interprets the epidermal growth factor as being a receptor tyrosine kinase ligand. The Examiner does not dispute the novelty of claims 3-5, 7, 13-14, 20, 21, and 23 over Lee. Thus, Applicants submit that the subject matter of claim 3 has been incorporated into claims 30-32 and the subject matter of claims 13 and 14 has been incorporated into claim 33. Thus, based on the above, Applicants submit that Lee does not anticipate the present claims and respectfully request that the rejections under 35 U.S.C. § 102(3) be withdrawn.

Conclusion

In view of the above amendments and remarks hereto, Applicants believe that all of the Examiner's rejections set forth in the May 18, 2009 Office Action have been fully overcome and that the present claims fully satisfy the patent statutes. Applicants, therefore, believe that the application is in condition for allowance. The Director is authorized to charge any fees or overpayment to Deposit Account No. 02-2135.

The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,

By 

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RBM/AHH
Enclosure: Fig. 37 and Fig. 38A-C of WO 2009/040134
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